REMARKS

The Official Action dated October 11, 2006 has been carefully considered. Entry of the Amendment dated July 6, 2006 is noted and appreciated. The present Amendment, taken with the following remarks, is believed sufficient to place the present application in condition for allowance. Reconsideration is respectfully requested.

By present amendment, independent claims 1, 13 and 14 have been amended and new claims 68 and 69 have been added. The independent claims are amended to clarify that the inventive peptides were derived from native apo A-IV, as disclosed, for example, on page 6, second paragraph. In addition the amino acid sequence length language was omitted in favor of changing the transition term to "consisting of" in order to clarify that the recited portions of the inventive peptides are the material active agents with respect to the function as disclosed and recited. Claim 65 was amended to clarify that there may be embodiments where the carrier molecule is not necessarily a carrier protein, while new claim 68 is added to capture the specific embodiment of a carrier protein, specifically. Support for these changes is found, inter alia, at page 6, fourth paragraph. Support for the subject matter of new claim 69 is found, for example, at page 7, paragraph 1 of the present specification. As it is believed that none of these changes involve the addition of new matter, entry is in order and is respectfully requested.

Claims 1, 4-14, 19 and 64-69 are currently pending and subject to examination.

35 U.S.C. § 112, first paragraph, "written description"

The previous rejection of claims 1, 4-14, 19 and 64 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a

way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, has been maintained. Specifically, the Examiner asserts that claims 1, 4-14, 19 and 64 encompass subject matter that is not defined in the specification. According to the Examiner, the claims are drawn to a method for inhibiting lipid oxidation associated with a condition in a patient, comprising administering to a patient a composition comprising a pharmacologically effective amount of an apolipoprotein (apo) A-IV peptide, to inhibit lipid oxidation, and that "the claimed invention asserts that the apo A-IV is a peptide sequence of from 6-71 amino acids in length and wherein the peptide has substantially the same lipid oxidation properties as the apo A-IV molecule. The Examiner notes the present teachings at page 6 discussing the peptides made from apo A-I, their properties, and their efficacy in treating atherosclerosis, but asserts that the specification does not describe the specific structure and function of these sequence fragments. The Examiner asserts that an A-IV peptide sequence of from 6-71 amino acids would encompass several variants of amino acids in lengths, and that "6-71 amino acids in length" does not give " a clear definition, whether the sequence is derived from a native apolipoprotein A-IV," and states that a sequence identifier has not been given to this sequence.

With respect particularly to claim 4, the Examiner asserts that the specification only "provides a generic description of how a variety of variants or fragments can be generated, and that no specific guidance is provided on generation of variants or fragments that demonstrate biological activity of the peptide sequence of SEQ ID NO 5." Broadly, the Examiner maintains that a person of skill in the art would not recognize from the disclosure that the applicant was in possession of the apolipoprotein AIV, which "comprises variants and fragments, which have substantially the same oxidation properties as the apolipoprotein

AIV wild type molecule," and that "there is no written description of either a representative number of the variants or of a common structural feature of the native apo A-IV that encompasses all the variants."

Responding to previous arguments by Applicants, the Examiner asserts that the arguments are not found persuasive because "the specification does not provide a description of '6-71' amino acids that includes specific structure and function of these fragments." The Examiner notes particular text from the present disclosure at page 12 wherein lipid oxidation inhibiting peptides of 5-90 amino acids in length, "which substantially correspond in sequence to amino acid sequence [sic] found in specific portions of apo A-IV, to which amino acids sequence of the claimed peptides correspond." The Examiner objects that "the sequence of that portion cannot be correlated to any claimed peptide sequence as no characteristics are provided nor any evidence to demonstrate retention of function with regard to inhibitory activity in lipid oxidation."

This rejection is traversed and reconsideration is respectfully requested.

Instant independent claim 1 is directed to a method for inhibiting lipid oxidation associated with a condition in a patient. The method comprises: administering to a patient a composition comprising a pharmacologically effective amount of a peptide derived from native apolipoprotein A-IV, wherein the peptide consists essentially of an amino acid sequence substantially corresponding to at least one of the sequences set forth as: SEQ ID NO:1; SEQ ID NO:2; SEQ ID NO:3; SEQ ID NO: 4; SEQ ID NO:5; SEQ ID NO:6; SEQ ID NO:7; SEQ ID NO:8; SEQ ID NO:9; SEQ ID NO:10; SEQ ID NO:11; SEQ ID NO:12; and SEQ ID NO:13, wherein the peptide has substantially the same lipid oxidation properties as an apolipoprotein A-IV molecule.

Instant independent claim 13 is directed to a method of inhibiting the progression of atherosclerosis in a patient in need thereof. The method comprises administering to the patient a composition comprising an effective anti-oxidation amount of a peptide derived from native apolipoprotein A-IV, wherein the peptide consists essentially of an amino acid sequence substantially corresponding to at least one of the sequences set forth as: SEQ ID NO:1; SEQ ID NO:2; SEQ ID NO:3; SEQ ID NO: 4; SEQ ID NO:5; SEQ ID NO:6; SEQ ID NO:7; SEQ ID NO:8; SEQ ID NO:9; SEQ ID NO:10; SEQ ID NO:11; SEQ ID NO:12; and SEQ ID NO:13, wherein the peptide has substantially the same lipid oxidation properties as an apolipoprotein A-IV molecule.

Instant claim 14 is directed to a method of treating a patient for atherosclerosis. The method comprises administering to the patient a composition comprising an effective anti-oxidation amount of a peptide, wherein the peptide consists essentially of an amino acid sequence substantially corresponding to at least one of the sequences set forth as: SEQ ID NO:1; SEQ ID NO:2; SEQ ID NO:3; SEQ ID NO: 4; SEQ ID NO:5; SEQ ID NO:6; SEQ ID NO:7; SEQ ID NO:8; SEQ ID NO:9; SEQ ID NO:10; SEQ ID NO:11; SEQ ID NO:12; and SEQ ID NO:13, wherein the peptide has substantially the same lipid oxidation properties as an apolipoprotein A-IV molecule.

The present specification teaches that the compounds of the present invention "show the capability to prevent and/or delay the oxidative modification of the LDL," by effective scavenging of peroxylic radicals" (page 4, lines 11-14). It is further disclosed that the inventive peptides are derived from apolipoprotien A-IV and "comprise specific portions of the native apo A-IV protein" so that there "should be no immunogenicity problems associated with their administration to humans" (page 6, lines 6-8). The inventive peptides comprise "at

least a six amino acid sequence derived from the amino terminal portion of the mature apolipoprotein A-IV, and that larger peptides of 15 and 90 amino acids each also containing the aforementioned repeat sequence, are also within the scope of the invention (page 6, lines 11-13). Regardless of the length of the peptide molecule, the claims make it clear that the scope of the invention is defined by peptides derived from apo A-IV and having the recited sequences and exhibiting the recited functioning. The addition of other peptides to the active portion, which are inconsequential to the functioning of the inventive peptide, do not take a given peptide out from under the scope of the present invention, and may or may not be present.

Applicants claim precisely defined actives and have eliminated language which may be interpreted as directed to non-expressly defined and supported peptides. Applicants are not aware of any patentability requirement for data demonstrating clinical efficacy, as such data is typically not available until drug agents reach a certain level in the governing regulatory scheme. Nonetheless, as disclosed, Applicants have derived peptides having these sequences and confirmed their activity with respect to the intended functioning, as noted in the present disclosure. Hence, the methods defined by the independent claims are fully supported by the present disclosure.

With respect in particular to claim 4, Applicants believe that the "consisting essentially of" transition term and length element are sufficient to overcome the Examiner's concerns regarding assertedly unsupported fragments. Any "fragment" within the scope of the independent claims must necessarily consist of one of the recited sequences, or a sequence substantially corresponding thereto, and must exhibit the recited function. "Thousands" of undefined fragments are not contemplated as within the scope of the present

claims. Claim 4 is directed to a specific species of the inventive peptide that is expressly supported by the specification, including by a precise statement of the sequence and submission of this sequence in a requisite Sequence Listing. The term "substantially corresponds" is used throughout the present specification and is expressly defined (e.g. page 22, lines 19-21)) as an amino acid sequence having approximately 70% homology to a specifically recited amino acid sequence.

As support for the subject matter of independent claims 1, 13 and 14 does not rely on structural correlates, but, rather, relies on express objective disclosure of the specifically recited species, Applicants submit that these claims, and claims dependent therefrom, are fully supported by the written description in the specification. The predictability of the *structure* of the peptide from the recited amino acid sequences is not a factor, as Applicants submit that such structure is inherent from the sequence and has not been disclosed as being necessary to determine prior to establishing efficacy. If a practitioner of the art modifies the inventive compounds such that intended functioning is not retained, then that compound is not within the scope of the present claims even if the presently recited sequence portions are present. Applicants believe this moots the Examiner's concerns of overbreadth and lack of support. Applicants are not aware of any requirement that patentability of a peptide or of methods employing specific peptides to exploit a recited function is dependent on disclosure or even determination of the structure of the peptide. Hence, the rejection of claims 1, 4-14, 19 and 64-66 under 35 U.S.C. §112, first paragraph, has been overcome. Reconsideration is therefore respectfully requested.

35 U.S.C. § 112, first paragraph "enablement"

Claims 1, 4-14, 19 and 64 are rejected under 35 U.S.C. § 112, first paragraph. The Examiner asserts that the specification, while being enabling for a method for inhibiting lipid oxidation associated with a condition in a patient comprising administering an apo A-IV compound, does not reasonably provide enablement for a method of inhibiting lipid oxidation comprising administering "all apo A-IV variants/fragments," such that the specification does not enable persons skilled in the art to make and/or use the invention commensurate in scope with the claims, without undue experimentation. This rejection is traversed and reconsideration is respectfully requested.

Recitations of independent claims 1, 13 and 14 are set forth in detail, above.

Applicants reiterate their appreciation of the Examiner's acknowledgement that the present disclosure is "enabling for a method for inhibiting lipid oxidation associated with a condition in a patient comprising administering an apo A-IV compound." Applicants further believe that the remaining objection of the Examiner, that is, that the disclosure allegedly does not reasonably provide enablement for a method of inhibiting lipid oxidation comprising administering "all apo A-IV variants/fragments," has been overcome by the instant amendment to the independent claims which eliminates the open-ended "comprising" language and eliminates the amino acid length range recitation with respect to the peptides employed in the inventive methods.

With respect to enablement, that is, whether an ordinary artisan may practice the present invention without undue experimentation, the specification provides ample guidance on the synthesis of the recited peptide actives and further notes that these peptides, derived from native apo A-IV, retain efficacy with respect to inhibition of lipid oxidation. Guidance on production of a pharmaceutical preparation, routes of administration, and efficacy with

respect to doses is also provided. Hence, an ordinary practitioner merely needs to apply knowledge readily available in the art to employ the presently disclosed peptides in the presently disclosed methods in order to achieve the desired benefit.

Applicants also appreciate the Examiner's acknowledgment that the guidance provided is sufficient with respect to the expressly recited sequences. The Examiner also acknowledges that enablement under § 112, paragraph one, in the case of pharmaceutical arts, does not require disclosure of clinical parameters or working examples of drug administration, but that the Examiner's concerns stem from asserted lack of guidance and undue experimentation associated with the myriad "fragments and variants" theoretically encompassed by the claim language, such that the rejection is based on an asserted lack of guidance with respect to employment of "fragments or variants" in the inventive methods (see Office Action April 6, 2006). Applicants submit that the present amendment, whereby the open transition phrase is replaced with "consisting essentially of," which acts to limit the scope to the specified sequences and any additional amino acids that do not materially affect the recited functioning of the peptide as employed in the present invention, eliminates the Examiners concern over unsupported "fragments or variants," by narrowing the scope of the inventive methods to those methods employing the specifically expressed, fully disclosed, supported, and enabled novel peptides.

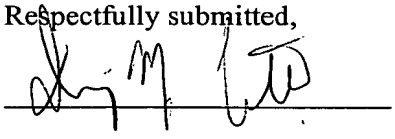
The enablement requirement of §112, first paragraph, as judicially interpreted by case law, requires that the specification must provide sufficient teaching such that one skilled in the art could make and use the full scope of the invention without undue experimentation. *CFMT, Inc. v. Yieldup Int'l Corp.*, 68 USPQ2d 1940, 1944 (Fed. Cir. 2003); *In re Wands*, 8 USPQ2d 1400, 1405 (Fed. Cir. 1988). "The key word is 'undue,' not experimentation.'"

Wands, 8 USPQ2d at 1405 (citation omitted). That is, the specification need only teach those aspects of the invention that one skilled in the art could not discern without undue experimentation. *Nat'l Recovery Techs., Inc. v. Magnetic Separation Sys., Inc.*, 49 USPQ2d 1671, 1673 (Fed. Cir. 1999) ("The scope of enablement ...is that which is disclosed in the specification plus the scope of what would be known to one of ordinary skill in the art without undue experimentation"); *Wands*, 8 USPQ2d at 1404-1405 ("Enablement is not precluded by the necessity for some experimentation such as routine screening."). It is well established PTO practice to consider novel methods employing novel pharmaceutical actives enabled without recitation of clinical results, as the governing regulatory scheme restricts such experimentation. Nonetheless, the instant specification discloses dosing and administrative route guidance in line with analogous peptide actives, systemic administration, and desirable peripheral action modes. Applicants submit that it is within the ability of a person of ordinary skill in the protein arts to employ the presently recited apo A-IV peptides in the inventive methods to achieve the desired benefit as stated in the present specification and as supported by the examples and data disclosed therein.

Hence, the rejection of claims 1, 4-14, 19 and 64, under 35 U.S.C. §112, first paragraph, for lack of enablement by the specification has been overcome. Reconsideration is respectfully requested.

It is believed that the above represents a complete response to the Examiner's rejection of the claims under 35 U.S.C. §§112, first paragraph, "written description" and "enablement" clauses, and places the present application in condition for allowance. Reconsideration and an early allowance are requested.

Respectfully submitted,



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